CLAIMS

We Claim:

1. A method for determining a T-cell epitope of a protein, wherein said protein is a bone morphogenetic protein (BMP), comprising the steps of:

(a) obtaining from a solution of dendritic cells and a solution of naïve CD4+ and/or CD8+ T-cells from a single human blood source;

(b) differentiating said dendritic cells, in said solution of dendritic cells, to produce a solution of differentiated dendritic cells;

(c) preparing a pepset of peptides from said protein;

(d) combining said solution of differentiated dendritic cells and said naïve CD4+ and/or CD8+ T-cells with said pepset, wherein said pepset comprises said T-cell epitope; and

(e) measuring the proliferation of said T-cells in said step (d).

2. The method of Claim 1, wherein said protein is selected from the group consisting of BMP-7 and BMP-14.

3. The method of Claim 1, wherein said pepset comprises a peptide having the sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5.

4 The method of Claim 1, wherein said pepset comprises a peptide having the sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8.

5. The method of Claim 1, further comprising the step of modifying said protein to produce a variant protein, wherein said variant protein exhibits an altered immunogenic response as compared to said protein.

6. A peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8.

7. A method of reducing the immunogenicity of a protein, wherein said protein is a bone morphogenetic protein, comprising the steps of:

(a) identifying at least one T-cell epitope in said protein by

(i) contacting an adherent monocyte-derived dendritic cell that has been differentiated by exposure to at least one cytokine *in vitro*, with at least one peptide comprising said T-cell epitope; and

(ii) contacting said dendritic cell and said peptide with a naïve T-cell, wherein said naïve T-cell has been obtained from the same source as said adherent monocyte-derived dendritic cell, and whereby said T-cell proliferates in response to said peptide; and

(b) modifying said protein to neutralize said T-cell epitope to produce a variant protein, such that said variant protein induces less than or substantially equal to the baseline proliferation of said naïve T-cells.

8. The method of Claim 7, wherein said T-cell epitope is modified by substituting a portion of the amino acid sequence of said T-cell epitope with an analogous sequence from a homolog of said protein.

9. The method of Claim 7, wherein said T-cell epitope is modified by substituting the amino acid sequence of said T-cell epitope with a sequence which substantially mimics the major tertiary structure attributes of said T-cell epitope.

10. The method of Claim 7, wherein said protein is selected from the group consisting of BMP-7 and BMP-14.

11. The method of Claim 7, wherein said epitope region comprises an amino acid sequence, wherein said amino acid sequence is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8.

12. A method for producing a variant protein having reduced allergenicity comprising the steps of:

a) obtaining a naturally-occurring protein, wherein said naturally-occurring protein is a bone morphogenetic protein, and preparing fragments of said naturally-

occurring protein;

b) contacting said fragments of said naturally-occurring protein with a first solution comprising naïve human CD4+ or CD8+ T-cells and differentiated dendritic cells;

c) identifying an epitope region of said naturally-occurring protein, wherein said identifying comprises measuring the ability of said fragments of said naturally-occurring protein epitope region to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells; and

d) modifying at least one amino acid in said epitope region identified in step c), to produce said variant protein.

13. The method of Claim 12, further comprising the step of comparing the ability of said fragments of said naturally-occurring protein to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells with the ability of said fragments of said variant protein to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells.

14. The method of Claim 12, wherein said protein is a bone morphogenetic protein.

15. The method of Claim 14, wherein said bone morphogenetic protein is selected from the group consisting of BMP-7 and BMP-14.

16. The method of Claim 12, wherein said epitope region comprises an amino acid sequence, wherein said amino acid sequence is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8.